# COMMONWEALTH OF AUSTRALIA

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### Warning

CHARLES DARWIN UNIVERSITY

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|---|---|
| **Family Name** | |
| **Given Names** | |
| **Student Number** | |
| **Teaching Period** | Semester 1, 2016 |

| **FINAL EXAMINATION** | **DURATION** |
|---|---|
| **PHA310 – Clinical Pharmacokinetics** | Reading Time: **10** minutes<br>Writing Time: **180** minutes |

## INSTRUCTIONS TO CANDIDATES

The examination has 2 Sections (A and B):

Section A contains Forty (40) Multiple Choice Questions. Answer all questions on the Faculty/School supplied Multiple Choice Answer Sheet. Total marks allocated: Forty (40). Suggested time allocation: One hour (60 minutes).

Section B contains Six (6) Calculation Questions. Answer all questions in the 20-page Booklet provided. Total marks allocated: Eighty (80). Suggested time allocation: Two hours (120) minutes.

**Total marks for this exam paper: 120**

## EXAM CONDITIONS

**You may begin writing from the commencement of the examination session.** The reading time indicated above is provided as a guide only.

This is a CLOSED BOOK examination

Any non-programmable calculator is permitted

No handwritten notes are permitted

No dictionaries are permitted

| ADDITIONAL AUTHORISED MATERIALS | EXAMINATION MATERIALS TO BE SUPPLIED |
|---|---|
| No additional printed material is permitted | 1 x 8-Page Book<br>1 x 20-Page Book<br>1 x Scrap Paper<br>Faculty/School Multiple Choice Answer Sheet<br>Formula Sheet/s<br>Graph Papers |

# THIS EXAMINATION IS PRINTED DOUBLE-SIDED.

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## Section A
## Multiple Choice Questions
## Total No of Marks for this section: 40

This section should be answered on the Faculty/School Multiple Choice Answer Sheet provided.

Please ensure that your name and student number have been written on the examination paper and the answer sheet.

Suggested Time allocation for Section A: 60 mins

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***End of Section A***

**Section B**
**Calculation Questions**
**Total Marks for this section: 80**
**Answer ALL (6) questions**

This section should be answered in the 20-page Answer Booklet provided.
Marks for each question are indicated.
Suggested Time allocation for Section B: 120 mins

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**Question 1 (8 marks)**

Ms HT is receiving 350mg of an antibiotic as repeated IV infusions (for 1 hour) every 8 hours to treat her infection. Assuming the clearance of gentamicin is 7.2L/hr with an elimination half-life ($t_{½}$) of 3 hours:

a Calculate the plasma concentration of gentamicin in Ms HT after the first IV infusion.

(2 marks)

b Calculate $C_{max}$, $C_{min}$ and $C_{ss}$ of gentamicin in Ms HT at steady-state.

(6 marks)

**Question 2 (22 marks)**

After a single IV bolus dose of 100mg of drug Y, the following data were obtained:

| Time (hr) | Plasma Concentration (mg/L) |
|---|---|
| 0.25 | 43.00 |
| 0.5 | 32.00 |
| 1.0 | 20.00 |
| 1.5 | 14.00 |
| 2.0 | 11.00 |
| 4.0 | 6.50 |
| 8.0 | 2.80 |
| 12.0 | 1.20 |
| 16.0 | 0.52 |

a Using the method of residuals, calculate the following parameters: $t_{½\alpha}$, $t_{½\beta}$, $k_{12}$, $k_{21}$, $k_{10}$, $V_c$, $V_{d\beta}$, $V_{dss}$, AUC and $CL_T$.

(20 marks)

b What will be the amount of the drug remaining in the body after 15h?

(2 marks)

**Question 3 (14 marks)**

a A 32-year-old 70kg male with generalised tonic-clonic seizures is being treated with phenytoin. Assuming Michaelis-Menten parameters of $V_{max}$ = 500g/d and $K_m$ = 4mg/L, calculate a dose of phenytoin that will achieve a steady-state concentration ($C_{ss}$) of 15mg/L.

(2 marks)

b Mr AT, a 50-year-old 75kg male, was prescribed a daily oral dose of 260mg phenytoin to control his simple partial seizures. After 1 month of therapy, his serum steady-state concentration was measured at 5mg/L. Since this was insufficient to control his seizures, his daily oral phenytoin dose was increased to 240mg b.d. (i.e. twice daily). One month after starting this new dosage regimen, Mr AT developed lateral-gaze nystagmus and his serum phenytoin concentration was found to be 24mg/L. Assuming that the volume of distribution of phenytoin is 0.7L/kg and the absolute bioavailability of oral phenytoin is 100%:

i. Use the direct linear plot (Mullen Method – with proper labels) to determine the $V_{max}$ and $K_m$ for phenytoin in Mr AT.

(6 marks)

ii. Recommend a dosage regimen to maintain steady-state plasma phenytoin concentration around 15mg/L (therapeutic range 10-20mg/L).

(2 marks)

iii. What will be the half-life ($t_{½}$) of phenytoin at steady-state if a dose of 200mg every 12 hours was given to Mr AT?

(4 marks)

**Question 4 (12 marks)**

After oral administration of a single dose of drug X, the following drug plasma-concentration were measured:

| Time (hr) | Drug concentration (μg/mL) |
|---|---|
| 0 | 0 |
| 1 | 3.13 |
| 2 | 4.93 |
| 3 | 5.86 |
| 4 | 6.25 |
| 5 | 6.28 |
| 6 | 6.11 |
| 8 | 5.45 |
| 10 | 4.66 |
| 16 | 2.67 |
| 24 | 1.20 |
| 32 | 0.54 |
| 48 | 0.10 |

Assuming the elimination rate constant is $0.1hr^{-1}$, estimate the absorption rate constant ($k_a$) using the Wagner-Nelson method.

**Question 5 (12 marks)**

After a single IV bolus administration of 50mg of drug Y, the plasma concentrations obtained were shown in the following table. The terminal rate constant for the decline in drug concentration (λ) is $0.1h^{-1.}$ Calculate the MRT, clearance and $V_{dss}$.

| Time (hr) | Concentration (μg/L) |
|---|---|
| 0 | 250 |
| 1 | 225 |
| 3 | 185 |
| 6 | 135 |
| 9 | 105 |
| 12 | 77 |
| 18 | 40 |
| 24 | 22 |

**Question 6 (12 marks)**

a A 50-year-old 70kg male (178cm in height) was presented to the hospital with atrial fibrillation. After his serum creatinine concentration was determined (79.6μmol/L), digoxin therapy was initiated to control his ventricular rate.

i. Calculate the loading dose (IV bolus) required (as digoxin has a very long half-life) to control his ventricular rate if the desired plasma digoxin concentration is 1.2ng/mL.

(6 marks)

ii. Calculate the digoxin maintenance dose (IV bolus) for this patient (in μg/day).

(2 marks)

b Mr TP (50 years old, 70kg and 178cm) is being treated with digoxin for NYHA Class III moderate heart failure. His current serum creatinine concentration is 309.4μmol/L. Calculate an oral digoxin maintenance dose (in μg/day) for Mr TP (F=0.7, ideal plasma concentration = 0.8ng/mL).

(4 marks)

***End of Section B***

***End of Exam Paper***